Atypical presentation of granulomatosis with polyangiitis: a case report and review of the literature

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Background: Granulomatosis with polyangiitis (GPA) is a systemic autoimmune disease characterized by necrotizing granulomatous vasculitis of the small- and medium-sized vessels. Classical GPA affects the upper and lower airways and kidneys. It commonly affects the nose and paranasal sinuses, middle and inner ear, and subglottic region of the larynx. Therefore, otolaryngological involvement is common in GPA and can sometimes be the initial presentation. In rare cases, otologic signs and symptoms can be the initial manifestations of this disease, including recurrent otitis media, otitis media with effusion, and sensorineural hearing loss.

Case Description: In the present study, we describe an atypical case of GPA of a 22-year-old female. The patient presented with severe and complicated otitis media with hearing loss and polyneuropathy (facial nerve paralysis and trigeminal nerve impairment), in addition to nasopharyngeal and parotid infiltration, in the absence of other otolaryngologic and systemic manifestations of GPA.

Conclusions: The diagnosis of GPA can be challenging due to its wide range of clinical manifestations. Otologic signs and symptoms are rare in this disease and can sometimes be the initial manifestations. Early diagnosis and treatment are important to prevent serious and permanent complications of the disease. Otolaryngologists should have high index of suspicion to systemic diseases such as GPA.

Keywords: Granulomatosis with polyangiitis (GPA); case report; complicated otitis media

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Introduction

Granulomatosis with polyangiitis (GPA) is a systemic autoimmune disease characterized by necrotizing granulomatous vasculitis of the small- and medium-sized vessels of the respiratory tract, kidneys, and other organs. It is a heterogeneous disease in terms of severity and clinical manifestations. The nasal cavity and paranasal sinuses are almost always involved (85–100%) (1). The prevalence of otologic involvement in GPA is variable (20–70%) (1-6).

In rare cases, otologic signs and symptoms can be the initial manifestations of this disease, including recurrent

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acute otitis media (AOM), otitis media with effusion (OME), and sensorineural hearing loss (1). Otitis media is one of the early symptoms or sequelae of GPA (7-12). The etiology and pathophysiology of GPA are not well known and have not yet been thoroughly investigated. The diagnosis is based on positive antineutrophil cytoplasmic autoantibody, cytoplasmic (c-ANCA) serology, histopathological confirmation of vasculitis, and granulomatous inflammation of the involved organ.

In the present study, we describe a case of bilateral complicated otitis media as the first manifestation of GPA and review the literature. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-24-47/rc).

Case presentation

A 22-year-old female, previously healthy, presented to our clinic complaining of bilateral hearing loss for one year. She also complained of bilateral aural fullness, non-pulsatile tinnitus, and left-sided nasal obstruction. She denied any other sinonasal or otologic symptoms. The patient had a history of persistent right middle ear effusion (MEE) a year prior to this presentation, for which she underwent myringotomy and ventilation tube insertion, which was extruded a month postoperatively. During the current presentation, examination showed bilateral MEE with a negative Rinne test bilaterally (*Figure 1*). Subsequent evaluation using transnasal nasopharyngoscopy revealed purulent discharge from the eustachian tube opening (*Figure 2*). Pure tone audiometry confirmed bilateral moderately severe conductive hearing loss (CHL). Neck computed tomography (CT) scan performed in another hospital showed nasopharyngeal fullness. The patient was diagnosed with recurrent bilateral OME and underwent bilateral myringotomy with T-tube insertion and nasopharyngeal biopsy. Nasopharyngeal biopsy revealed normal respiratory epithelium, whereas nasopharyngeal culture revealed a heavy growth of Staphylococcus aureus.

One month later, the patient presented with newly developed left-sided facial weakness for three days with severe left ear pain radiating to temples associated with hemoptysis and epistaxis. Examination revealed a discharging T-tube on the left side with a bulging tympanic membrane (TM) and a patent T-tube on the right. Grade IV facial weakness on the left side, left parotid swelling, palpable left level II lymph node, and decreased sensation on the left side of the face in all three divisions of the trigeminal nerve were also observed. Examination of other cranial nerves was unremarkable. Transnasal endoscopic examination revealed the same previous findings. Laboratory workup showed mild white blood cell (WBC) count elevation with elevated inflammatory markers. Brain CT revealed nasopharyngeal fullness on the left side with bilateral mastoid opacification (*Figure 3*). Brain magnetic resonance imaging (MRI) showed progression of the nasopharyngeal swelling, infiltration into the left parotid gland, and dural enhancement in the left Meckel's cave (*Figure 4*). Chest CT scan showed a central cavitary lesion in the right lower lobe. Technetium-99 bone scan followed by Gallium-67 bone scan did not demonstrate an active infectious process of the skull base.

The patient was admitted and was started on intravenous antibiotics, analgesia, and systemic steroids. Additional laboratory workup revealed elevated levels of c-ANCA (133.87 AU/mL). She underwent another examination of the nasal cavity and nasopharynx under general anesthesia, which revealed newly developed nasal polypoidal lesions (*Figure 5*). Multiple biopsies were obtained from the nasal lesions and nasopharynx, which showed necrotizing granulomatous inflammation upon histopathological examination. The patient was then diagnosed with GPA. The patient was started on prednisone 40 mg daily, methotrexate 10 mg weekly (for 36 weeks), and rituximab (once weekly for 4 weeks every 6 months) after rheumatology consultation. She improved significantly on medical management and was discharged with regular follow-ups in rheumatology and otolaryngology outpatient clinics. Levels of c-ANCA after treatment decreased to

Highlight box

Key findings

- Bilateral complicated otitis media.
- Polyneuropathy (facial nerve paralysis and trigeminal nerve impairment).
- Left-sided nasopharyngeal fullness and parotid infiltration.

What is known and what is new?

- Granulomatosis with polyangiitis (GPA) has wide range of clinical manifestations.
- Bilateral complicated otitis media as the first manifestation of GPA, which is rare.

What is the implication, and what should change now?

- Otolaryngologists should have high index of suspicion to systemic diseases.

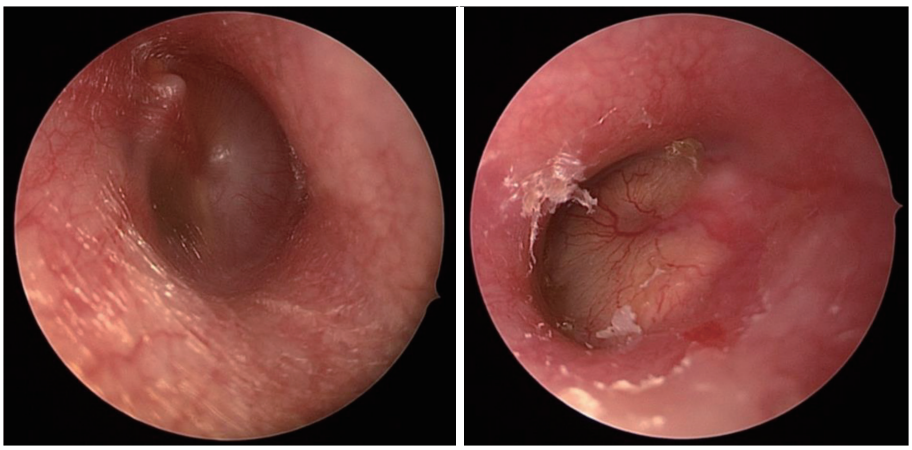

Figure 1 Ear endoscopy showing bilateral middle ear effusions.

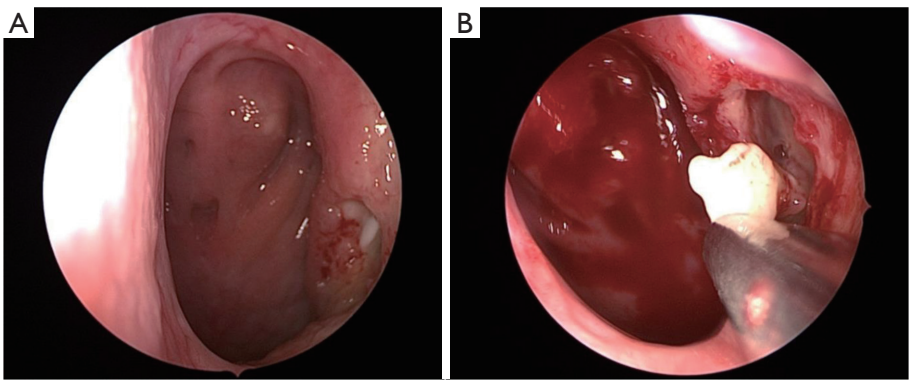

Figure 2 Trans-nasal endoscopic examination showing bilateral patent nasal cavities with left-sided nasopharyngeal fullness (A) and purulent discharge from the eustachian tube opening (B).

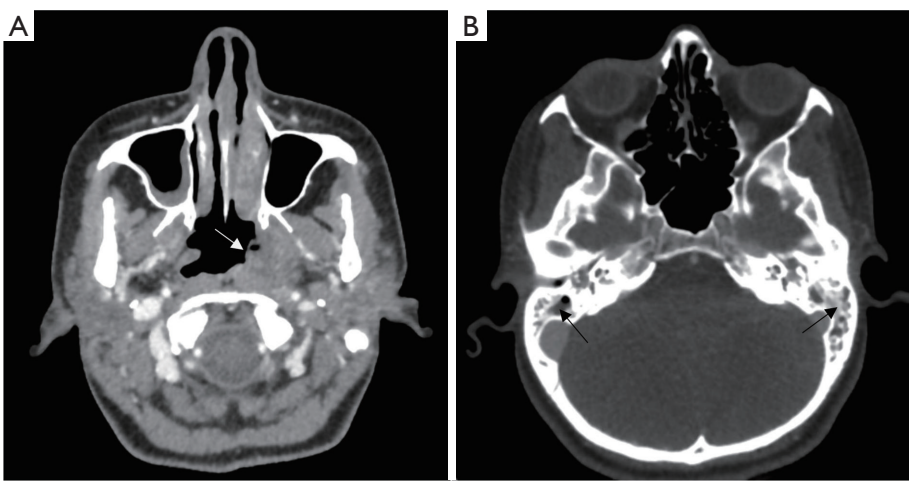

Figure 3 Brain computed tomography showing nasopharyngeal fullness on the left side (white arrow in A) with bilateral mastoid opacification (black arrows in B).

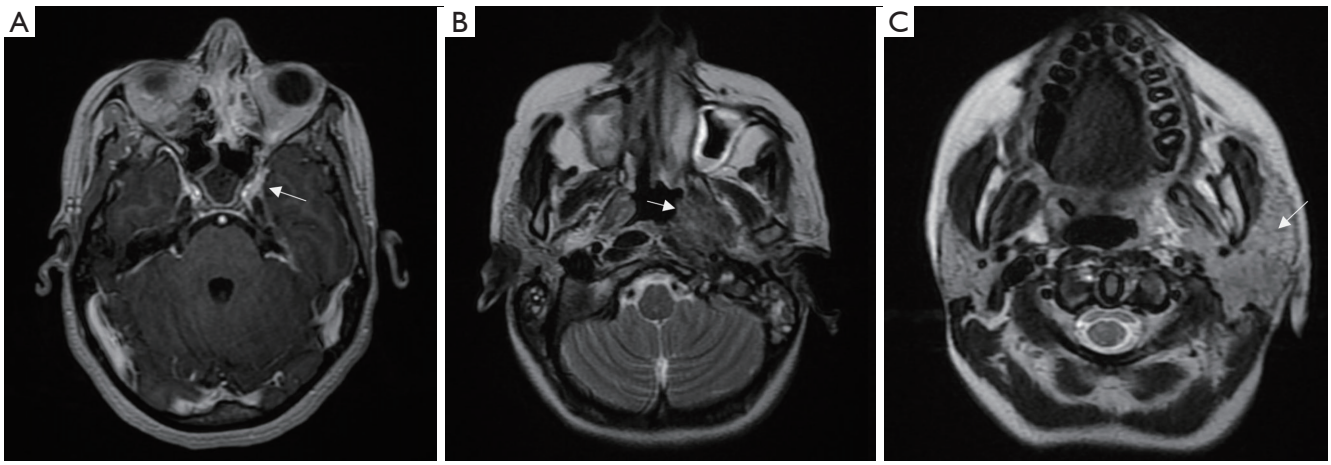

Figure 4 Contrasted axial T1 weighted brain magnetic resonance imaging showing dural enhancement in the left Meckel's cave (white arrow in A), T2 weighted brain MRI showing progression of the left nasopharyngeal swelling (white arrow in B) and infiltration into the left parotid gland (white arrow in C).

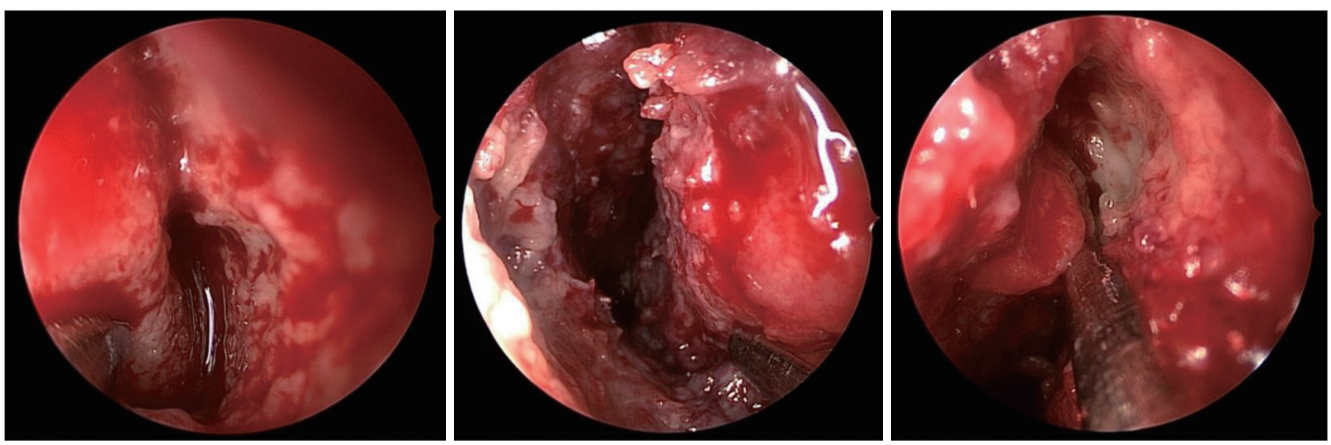

Figure 5 Examination of the nasal cavity and nasopharynx showing polypoidal lesions over the nasal septum and inferior turbinate, bilaterally.

5.30 AU/mL. The patient underwent nasal endoscopy with release of nasal adhesions and removal of bilateral T-tubes 6 months after discharge. After another six months, the patient reported resolution of otorrhea and otalgia; however, she continued to have moderate hearing loss. Examination revealed healed TMs with mild retraction bilaterally and mild improvement of facial nerve weakness (grade II). Hearing aids were prescribed for the residual hearing loss.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

GPA was first described as Wegener's granulomatosis in 1936 by Friedrich Wegener. It is a multi-systemic necrotizing non-caseating granulomatous vasculitis that affects small-medium arteries, capillaries, and veins.

Classical GPA affects the upper and lower airways and the kidneys, although other organs may also be involved. It commonly affects the nose and paranasal sinuses, middle and inner ear, and subglottic region of the larynx (1-4). The etiology and pathophysiology of GPA are not well-known and poorly investigated. What we know is that circulating pathologic antibodies, c-ANCA, attack small- and medium-sized blood vessels. It has an incidence rate of 1 in 25,000, with a mean age of 41 years. Approximately 90% of patients are Caucasians (2).

GPA has no well-defined diagnostic criteria, and its diagnosis is based on positive c-ANCA serology and histopathological confirmation of vasculitis and granulomatous inflammation of the involved organ (13). Positive c-ANCA has a specificity of 80–90% for GPA. However, c-ANCA can also be associated with other systemic diseases (1,14). Most cases demonstrate positive c-ANCA (90%), which also correlates with disease activity. A positive c-ANCA serology highly suggests GPA but can never replace histopathologic confirmation (13,15).

GPA is a heterogeneous disease in severity and clinical manifestations (16). Otolaryngological involvement is common in ANCA-associated vasculitis (AAV), particularly GPA, and is often an early feature of the disease. The nasal cavities are almost always involved. Nasal obstruction, crusting and purulent discharge, facial pain, septal perforation, and progressive nasal deformity are the most frequent nasal manifestations of GPA (17,18). Otologic manifestations are common in GPA (20–70%) and represent the second most frequent symptoms of head and neck involvement (3-5). The most common otologic symptom is CHL due to MEE (23–70%) (6). In GPA, if otitis media is left untreated, there is a risk of developing permanent sensorineural hearing loss (19). Localized GPA may present only with otologic signs and symptoms without evidence of involvement of other organ involvement (20). Facial nerve palsy has been reported in 5–8% of GPA cases (21-23). The otitis media with ANCA-associated vasculitis (OMAAV) working group, funded by the Japan Otologic Society, conducted a nationwide survey and reported the clinical characteristics and treatment outcomes of 235 patients with OMAAV (19). The major clinical manifestation was intractable OME that did not respond to standard treatment options, such as antibiotics and ventilation tube insertion, with significant deterioration of CHL. Female gender was predominant (71%) and facial palsy was frequent (32%). Therefore, patients with intractable and recurrent otitis media or associated facial palsy should be suspected to have GPA.

The treatment options for GPA localized to the upper respiratory tract and OMAAV have not yet been standardized. Due to the autoimmune nature of GPA, the combination of corticosteroids and immunosuppressive medications is the mainstay of treatment. Methotrexate is an alternative treatment option for less severe forms of GPA. In a systematic review conducted by Ashman *et al*., the primary treatment of GPA with otologic manifestations consisted mainly of systemic steroids and immunomodulation. Myringotomy with tube insertion, endoscopic sinus surgery, and local steroids were found to be adjunctive measures to alleviate local disease (24). Furthermore, Rituximab can be combined with steroids as first-line treatment for GPA with refractory otolaryngological manifestations (19,20). Intravenous immunoglobulin (IVIG) can decrease disease activity by interrupting T-cell- or B-cell-mediated immune responses (25). Early diagnosis and treatment are keys to managing GPA cases. GPA is rapidly progressive without treatment, with a 10% two-year survival rate. Appropriate medical treatment has dramatically increased long-term survival (26). Our patient's initial presentation did not suggest any systemic disease, and our treatment plan focused only on otologic symptoms. However, after histopathological confirmation of GPA, corticosteroids and immunosuppressive agents were initiated by rheumatology colleagues, resulting in a good response to the treatment plan to the point of remission.

Conclusions

The diagnosis of GPA can be challenging due to its wide range of clinical manifestations. Head and neck involvement is common in GPA and can sometimes be the initial presentation. Early diagnosis and treatment are important to prevent serious and permanent complications of the disease.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-24-47/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-24-47/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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